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ATTACHMENT A

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:	)	
	)	
PAUL A. LUCIW, ET AL.	)	Group Art Unit: 1813
	)	
Serial No. 08/089,407	)	Examiner: M. Woodward
	)	
Filed: July 8, 1993	)	Attorney Docket No. 0035.009

For: HIV IMMUNOASSAYS USING SYNTHETIC ENVELOPE POLYPEPTIDES (AS AMENDED)

DECLARATION

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

I, John A.T. Young, do hereby declare as follows:

1. I received my Ph.D. in Human Genetics from Imperial Cancer Research Fund and University College, London, United Kingdom in 1987 having previously received a B.S. in Biochemistry from the University of Dundee in 1983.

2. I am currently an Assistant Professor, Department of Microbiology and Molecular Genetics, Harvard Medical School. My Curriculum Vitae is attached as Exhibit 1.

3. I have read and understand Luciw et al. application Serial No. 08/089,407 and Luciw et al. application Serial No. 08/557,501 ('501) as well as the Office Action mailed January 23, 1996.

4. One of ordinary skill in the art in 1984 understood the term "synthetic peptide" to mean a peptide prepared by chemical synthesis. The term "synthetic" was used to describe a peptide synthesized by chemical means in numerous publications prior to the October 31, 1984 filing date of parent application Serial No. 06/667,501. Representative publications (there are still others) include Altman 1984, Barlow 1984, Billet 1984, Dale 1983, Green 1983, Hintz 1982, Hirayama 1982, Jacob 1983, Jolivet 1983, Lieu 1976, Morrow 1983, Morrow 1984, Muller 1983, Pacella 1983, Rothbard 1984, Rougon 1984, Sherwood 1983, Shi 1984, Sutcliffe 1983, Tamura 1982, and Wabuke-Bunoti 1984.[1] The articles were published in a variety of well-known journals, including those read by a general scientific audience (e.g., *PNAS* and *Science*) as well as those read mainly by virologists and immunologists (e.g., *Journal of Virology and Molecular Immunology*). These are the journals that one skilled in the art would be expected to review.

5. Following 1984, the term "synthetic" was still understood by those skilled in the art to mean a peptide synthesized by chemical means. This is illustrated by the following sentence taken from Chapter 5 under the sub-heading "Synthetic peptides" of a widely-circulated laboratory research manual (Harlow, E., and D. Lane. 1988. Antibodies: a laboratory manual. Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.): "Peptides are normally synthesized using the solid-phase techniques pioneered by Merrifield (1963)." The term is still so-understood today.

[1]The full citation for each of the references cited in this declaration is included in Exhibit 2.

6. The prior art was capable of making a clear distinction between a synthetic peptide (i.e. one synthesized by chemical means) and a peptide fragment generated by some other means. See, Dale 1983, Hirayama 1982, Liau 1975, Morrow 1983, Morrow 1984, Muller 1983, Rothbard 1984, and Sherwood 1983.

7. Prior to October 31, 1984 one skilled in the art was fully capable of synthesizing peptides of considerable length. Specific examples of synthetic polypeptides containing as many as 40 amino acids were reported in the art prior to October 31, 1984. Ten of the above-mentioned articles (Altman 1984, Barkas 1984, Dale 1983, Hirayama 1982, Jacob 1983, Muller 1983, Rothbard 1984, Shi 1984, and Wabuke-Bunoti 1984) report synthetic peptides (i.e.: peptides made by chemical synthesis) having lengths of from 15 to 24 amino acids and one article (Bellet 1984) reports a 37 amino acid synthetic peptide. Reid (1981) employed a 34 amino acid synthetic peptide, while Puett (1982) employed a 40 amino acid synthetic peptide.

8. Immunoassays employing synthetic peptides such as claimed in the subject application were known in the art in 1984. Those techniques included ELISA analyses which employed peptides immobilized on microtiter plates, test sera, and enzyme-coupled secondary antibodies (e.g. Altman 1984, Bellet 1984, Green 1983, Jolivet 1983, Rothbard 1984, Wabuke-Bunoti 1984). Those techniques also included solid-phase radioimmunoassays that employed immobilized synthetic peptides, test sera, and ^{125}I-labeled protein A (Jacob 1983, Morrow 1984, Pacella 1983, Rothbard 1984,). Other methods were also known in the art in 1984 for detecting specific interactions between synthetic peptides and antibodies including radioimmunoassays that employed

radioactively-labeled peptides or antibodies (e.g. Barkas 1984, Hintz 1982, Rougon 1984, Shi 1984, Tamura 1982).

9. The statement at page 3 of the '501 specification that "synthetic peptides may also be prepared" would have been understood by one of ordinary skill in the art in October 1984 as a teaching that such synthetic peptides would be used in the immunoassays described in the '501 specification. The '501 specification at pages 11, 14 and 15 specifically teaches that one use for the polypeptides of the invention is as antigens in a variety of immunoassays. One skilled in the art would not infer from the teaching of the patent specification that production of synthetic peptides would be a teaching of a useless act. One skilled in the art would be led to use the synthetic peptides in immunoassays just as the specification teaches.

10. The HIV nucleotide and amino acid sequences provided in the '501 parent application enabled one of ordinary skill in the art in October 1984 to identify synthetic HIV antigenic peptides, i.e., peptides containing an immunogenic amino acid sequence. To demonstrate this, I performed a hydrophilicity analysis of the ARV-2 Env sequence, according to the Hopp protocol (Hopp 1981, Hopp 1983). The directions in Hopp, together with the hydrophilicity values given in Hopp 1981, permit a straightforward analysis that was easily within the skill of the art in October 1984. The confirmation of antigenicity was also within the skill of the art in 1984. An antigen could be screened by using it in an immunoassay such as the prior art immunoassays identified in Paragraph 8 and testing it with sera of patients known to be infected. This screening process is the technique that is, in fact, disclosed in the Hopp references.

11. Employing the Hopp protocol, the most hydrophilic region of ARV-2 Env, was identified as residues 738-743 (ERDRDR). Synthetic peptides derived from HIV Env that contain these amino acid residues are recognized by a proportion of AIDS patient antisera as demonstrated by later actual tests. (Broliden 1992, Goudsmidt 1990, Kennedy 1986). The second-most hydrophilic region was identified as residues 653-658 (EKNEQE). Synthetic peptides containing this region of HIV Env are also recognized by sera from HIV infected individuals (Broliden 1992, Goudsmit 1990, Krowka 1991). The third most hydrophilic region of ARV-2 Env, residues 739-738 (EEEGGE), overlaps the first hydrophilic region. Synthetic peptides containing this third region of HIV Env are recognized by sera from HIV infected individuals. (Broliden 1992, Goudsmidt 1990, Kennedy 1986). The region containing residues 505-510 (QREKRA) was also identified as being highly hydrophilic. This finding was noted using the same computer analysis by Pauletti (1985). Synthetic peptides derived from HIV Env containing all or most of these residues are recognized by AIDS patient antisera (Broliden 1992, Kennedy 1987, Krowka 1991, Meshcheryakova 1993, Palker 1987, Steckert 1992).

12. Employing the Hopp protocol, the most hydrophilic region of ARV-2 Gag, was identified as residues 102-107 (EKIEEE). Synthetic peptides derived from HIV Gag that contain these amino acid residues are recognized by a proportion of AIDS patient antisera as demonstrated by later actual tests. (Jiang 1992). The second-most hydrophilic region was identified as residues 109-114 (NKSKQQ). Synthetic peptides containing this region of HIV Gag are immunogenic and are recognized by sera from HIV infected individuals (Jiang 1992).

13. The HIV sequences provided in the '801 parent application also enabled one of ordinary skill in the art in October, 1984 to identify antigenic HIV Env linear epitopes by still other techniques. One other approach known in the art, was to generate one or a panel of several synthetic peptides derived from the polypeptide sequence and test each peptide for antibody reactivity. The generation of one or a panel of synthetic polypeptides from a single protein was a routine matter in 1984.

14. A panel of eight peptides (each 13-15 amino acids in length) of interleukin-2 was generated by Altman (Altman 1984) and a panel of five synthetic peptides (8 to 16 amino acids long) derived from adenovirus 19K and 53K proteins was generated by Green. (Green 1983). In addition, Sutcliffe generated a panel of 12 peptides from MuLV polymerase gene and a panel of 18 peptides from the rabies glycoprotein gene. (Sutcliffe 1983)

15. Prior to October 1984, those skilled in the art knew that a proportion of antibodies raised against native proteins could recognize epitopes contained on synthetic peptides derived from a protein sequence (Rombard 1984; Leach 1983) or contained on proteolytic protein fragments (Lando 1982).

16. Based on the information described herein, those skilled in the art could have, without undue experimentation, used the sequence of ARV-2 Env provided in the '501 application to generate synthetic peptides representing most of the HIV glycoprotein. These peptides could then have been tested using standard assays known in the art, and immunogenic regions of HIV Env identified.

17. I have reviewed in detail Montagnier, *Science*, 225, 63-66 (July, 1984) and Schupbach et al., *Science*, 224, 503-505 (May, 1984). In my opinion these articles would not have enabled one skilled in the art to prepare a synthetic HIV envelope polypeptide sequence for use in an immunoassay without undue experimentation. I conclude this for the following reasons:

so?

a) These articles did not provide any HIV nucleotide or amino acid sequence information.

b) Although HIV proteins were purportedly identified by immunoblotting in these publications, a person of ordinary skill in the art would not have been able to produce sufficient quantities of any of these viral proteins for sequencing. Sufficient quantities could not have been produced because cultures of primary human cells failed to produce significant quantities of HIV, as the virus is cytopathic and rapidly killed the infected virus-producing cells. Therefore, a person of ordinary skill in the art, attempting to generate sufficient quantities of HIV proteins for detailed characterization, would have i) had to obtain an appropriate established cell line known to produce HIV and ii) had to have a knowledge of the precise conditions required for infecting these cells and for maintaining the infected cells for long periods of time in culture.

data?

c) By October 31, 1984, the Gallo and Montagnier groups had reported cell lines that could be used to produce significant levels of HIV (Popovic 1984, Montagnier 1984). Gallo and Montagnier were world

why not?

leaders in HIV research at the time, and thus can hardly be considered to be of "ordinary skill in the art". At the time of the '501 application data, the precise origin of the cell line used by the Gallo group had not been disclosed (Popovic 1984). The Montagnier group used cells generated by fusion between HIV producing primary T cells and EBV-transformed B-cells (Montagnier 1984). It would not have been possible for a scientist of ordinary skill in the art to have used the same technique to produce cell lines that were identical to those described by the Montagnier group. Even if a scientist of ordinary skill in the art had attempted to obtain the cells described by the Gallo and Montagnier groups, I am not aware of any evidence that these cell lines were being distributed freely to the public at the time of the '501 application data. Furthermore, the precise culture conditions required for maintaining HIV-infected cells in culture had not been disclosed.

18. The announcement by the Gallo group that HTLV-III was related to HTLV-I and II, such as contained in Gallo et al. (1983) and Arya et al. (1984), led workers such as Chang to incorrectly presume that the Env gene was located at the same position in the HIV and HTLV-I and II genomes. Furthermore, the Gallo group proposed that the HIV genome contains a pX or LOR region similar to those found in HTLV-I and II. In fact, as the '501 application correctly disclosed, a) HIV is not closely related to HTLVs, b) the Env gene is not located at the same position in the HIV and HTLV genomes and c) there is no pX or LOR region in the HIV genome.

19. The presumption that HIV was closely related to HTLV-I and II led the Gallo group to seriously misidentify HIV envelope proteins:

a) The Gallo group described a 65 kD HIV protein as "envelope-related" apparently because it migrated on SDS-polyacrylamide gels at a position similar to that of the 62-65 kD HTLV precursor envelope protein (Schupbach 1984). The HIV precursor envelope protein is, however, a 160kD protein (designated gp160), a fact that only came to light after the '501 application filing date.

if true then what did Lucia know?

b) The Gallo group described a 41 kD HIV protein as "the presumed envelope antigen of the virus" (Samgadharan 1984). The 41 kD protein was shown to be an antigenic viral structural protein (Samgadharan 1984). However, the inescapable conclusion from this manuscript was that these workers presumed that this viral protein was envelope-related because it was similar in size to the 46kD HTLV envelope protein (gp46; Samgadharan 1984) i.e., the HIV p41 protein was equivalent to HTLV gp46. In fact, these proteins are not equivalent for the following reasons:

i) All retroviral envelope proteins are synthesized as precursor proteins (see ¶19a) that are cleaved into two mature subunits designated surface (SU) and transmembrane (TM). These two envelope proteins remain associated together after this cleavage and are incorporated together onto the surface of viral particles.

However, these proteins are structurally distinct and perform different functions during viral entry; the SU protein is primarily involved in receptor binding, whereas the TM protein contains the transmembrane region that anchors the envelope proteins on the virus surface. The TM protein is primarily involved at a step of viral entry following receptor binding.

ii) The SU and TM proteins of HIV are designated gp120 and gp41 (the 41 kD protein described by Sarngadharan 1984), respectively. The SU (gp120) protein of HIV was not described prior to the '501 application filing date.

iii) The SU protein of the HTLVs is gp46 and the TM protein of the HTLVs is p20E, a 20 kD protein.

20. I have also reviewed in detail Chang U.S. application Serial No. 659,339 filed October 10, 1984 including the partial DNA sequence of Figure 3. The Chang specification (1) incorrectly describes the location of the Env gene in the HIV genome, and (2) misrepresents the sequence of the Env gene which is purported to be encompassed (i.e. wholly-contained) within the DNA sequence shown in Figure 3. An individual skilled in the art attempting to identify the HIV Env open reading frame found in the sequence of Figure 3 would have been unable to do so.

21. Although Chang represents that the Figure 3 sequence "encompasses the *env* region" (p. 5, lines 1-2), that is incorrect. In fact, the Figure 3 sequence contains a

portion of the *pol* gene, the *sor* gene and only approximately one-third of the envelope gene.

22. Moreover, the Chang Figure 3 sequence includes an error. The Figure 3 sequence includes an extra nucleotide ("A") at position 2497, a residue which does not actually exist in the HIV envelope gene. This mistake leads to a +1 translational frameshift at this position in the partial sequence of the envelope open reading frame. As a consequence of this error, this open reading frame is only correct over the region encoding the first 63 amino acids of Env (including the N-terminal signal peptide which is removed during protein biosynthesis). The open reading frame of the Figure 3 sequence then continues with three amino acids encoded by an incorrect reading frame followed by a stop codon.

23. Based on Figures 1 and 2 of Chang, a scientist would have been completely misled about the placement of the envelope gene relative to restriction enzyme sites in the HIV genome, e.g., an EcoR1 site that is actually located upstream of the envelope gene is shown in the Chang '339 application both as contained within the envelope gene (Figure 1) and upstream of the envelope gene (Figure 2). Also, a Bgl II site, which is actually located in the envelope gene, is shown in the Chang application as within the "pX" region, a region which does not exist in the HIV genome. HIV is not closely related to HTLV-I and II, and unlike these other human retroviruses HIV certainly does not contain a pX region.

24. Based, *inter alia*, on the above-identified defects, Chang did not enable one skilled in the art in October, 1984 to grow, isolate and/or sequence the envelope gene of HIV.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: March 19, 1997 By: _____
John A.T. Young

CURRICULUM VITAE

PERSONAL

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Birthdate: February 28, 1961
Kirkcaldy, Fife, Scotland
Citizenship: United Kingdom
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ACADEMIC APPOINTMENTS

1992 to 1995 Assistant Professor
Department of Microbiology and Immunology
University of California, San Francisco
San Francisco, California

1992 to 1995 Assistant Investigator
Gladstone Institute of Virology and Immunology
San Francisco General Hospital
San Francisco, California

1992 to 1995 Member, Program in Biological Sciences (PIBS)
Cell Biology Program
University of California, San Francisco

1992 to 1995 Member, Biomedical Sciences Program
University of California, San Francisco

1995 to Assistant Professor
Department of Microbiology and Molecular Genetics
Harvard Medical School

1995 to Member, Biological and Biomedical Sciences Program,
Harvard Medical School

1995 to Member, Committee on Virology, Harvard Medical School

1995 to Member, Board of Tutors in Biochemical Sciences, Harvard University

POSTDOCTORAL TRAINING

1987-1989 EMBO Postdoctoral Fellow
Department of Microbiology and Immunology
University of California, San Francisco
Advisor: Harold E. Varmus, M.D.

1989-1992 Arthritis Foundation Postdoctoral Fellow
Department of Microbiology and Immunology
University of California, San Francisco
Advisor: Harold E. Varmus, M.D.

EDUCATION

1983 University of Dundee
Dundee, United Kingdom
B.Sc., Biochemistry (First Class Honours)

1987 Imperial Cancer Research Fund and University College
London, United Kingdom
Ph.D., Human Genetics
Thesis: Expression and Polymorphism of HLA-D Region Genes
Ph.D. Advisor: John Trowsdale, Ph.D.

TEACHING EXPERIENCE

1992 Co-organizer
Introduction to Cell Biology course
Medicine 412, UCSF

Discussion Leader
Cell Biology Course 212, UCSF

1993 Lecturer
The Biology of AIDS
Biomedical Sciences Minisymposium, UCSF

1993 Discussion Leader
Tissue Organization and Morphogenesis course
Biomedical Sciences 210, UCSF

Discussion Leader
Molecular Biology of Animal Viruses course
Microbiology 208, UCSF

1994 Lecturer, The Biology of Virus Infection course
Microbiology 208, UCSF

1996 Lecturer, Microbiology 201, Harvard Medical School
(4 lectures, 9 discussion groups)

1997 Co-director, Virology 200, Harvard Medical School

1997 Lecturer, Virology 200, Harvard Medical School (3 lectures)

COMMITTEES

1992 to 1995 Member, Dean's Advisory Committee to the UCSF AIDS Clinical Research Center

1993 to 1995 Member, Executive Committee of the UCSF Biomedical Sciences Program

1993 to 1995 Member, UCSF Student Research Committee

1996 to Member, Virology Admissions Committee, Harvard Medical School

1996 to Member, Division of Medical Sciences Curriculum Committee, Harvard Medical School

TRAINEES

1992 to 1995 Kurt Zingler
Ph.D. Thesis Student
Immunology Program, UCSF

Jürgen Brojatsch, Ph.D.
Postdoctoral Fellow

Carole Bélanger, Ph.D.
Postdoctoral Fellow
Fonds de la Recherche en Santé du Québec

1993 to 1995 Lynn Connolly
M.D., Ph.D. Thesis Student
Medical Scientist Training Program, UCSF

Morgan Jenkins, M.D.
Clinical Research Fellow
Universitywide AIDS Research Program

1996 to Heather B. Adkins
Ph.D. Thesis Student
Committee on Virology, Harvard Medical School

1996 to Vincent Solomon
Ph.D. Thesis Student
Biological and Biomedical Sciences, Harvard Medical School

PUBLICATIONS

1. Trowsdale, J., Young, J.A.T., Kelly, A.P., Austin, P.J., Carson, S., Meunier, H., So, A., Ehrlich, H.A., Spielman, R.S., Bodmer, J., and Bodmer, W. (1985) Structure, sequence and polymorphism in the HLA-D region. *Immunol. Rev.* 85:135-173.

2. Young, J.A.T. and Trowsdale, J. (1985) A processed pseudogene in an intron of the HLA-DPβ1 chain gene is a member of the ribosomal protein L32 gene family. *Nucl. Acids Res.* 13:8883-8891.

3. Trowsdale, J., Austin, P., Carson, S., Kelly, A., Lamb, J., and Young, J.A.T. (1985) Cloned HLA-D genes: Characterisation and approaches to expression and analysis of function. In: *Human T-cell Clones* (M. Feldmann, J.R. Lamb, and J.N. Woody, eds.), The Human Press, pp 49-57.

4. Bodmer, W.F., Trowsdale, J., Young, J., and Bodmer, J. (1986) Gene clusters and the evolution of the major histocompatibility complex. *Phil. Trans. R. Soc. Lond.* 312:303-315.

5. Young, J.A.T., Wilkinson, D., Bodmer, W.F., and Trowsdale, J. (1987) Sequence and evolution of HLA-DR7 and HLA-DRw53-associated β chains. *Proc. Natl. Acad. Sci. USA* 84:4924-4933.

6. Bodmer, J., Bodmer, W., Heyes, J., So, A., Tonks, S., Trowsdale, J., and Young, J. (1987) Identification of HLA-DP polymorphism with DPα and DPβ probes and monoclonal antibodies: Correlation with primed lymphocyte typing. *Proc. Natl. Acad. Sci USA* 84:4596-4600.

7. Young, J.A.T., Lindsay, J., Bodmer, J.G., and Trowsdale, J. (1988) Epitope recognition by an HLA-DPα chain-specific monoclonal antibody (DP11.1) is influenced by the association of the DPα chain and its polymorphic DPβ chain partner. *Hum. Immunol.* 23:37-44.

8. Young, J.A.T. (1988) HIV and HLA similarity. Scientific correspondence. *Nature* 333:215.

9. Young, J.A.T. and Trowsdale, J. (1990) The HLA-DNA gene is expressed as a 1.1kb mature mRNA species. *Immunogenetics* 31:386-388.

10. Young, J.A.T., Bates, P., Willert, K., and Varmus, H.E. (1990) Efficient incorporation of human CD4 protein into Avian Leukosis Virus particles. *Science* 250:1421-1423.

11. Young, J.A.T., Bates, P., and Varmus, H.E. (1993) Isolation of a chicken gene that confers susceptibility to infection by subgroup A avian leukosis and sarcoma viruses. *J. Virol.* 67:1811-1816.

12. Bates, P., Young, J.A.T., and Varmus, H.E. (1993) A receptor for subgroup A Rous sarcoma virus is related to the low density lipoprotein receptor. *Cell* 74:1043-1051.

13. Connolly, L., Zingler, K., and Young, J.A.T. (1994) A soluble form of a receptor for subgroup A avian leukosis and sarcoma viruses (ALSV-A) blocks infection and binds directly to ALSV-A. *J. Virol.* 68:2760-2764.

14. Young, J.A.T., Bates, P.F., and Varmus, H.E. (1994) A protein related to the LDL receptor is a cellular receptor specific for subgroup A-avian leukosis and sarcoma viruses. *In:*

Receptor-mediated Virus Entry into Cells. (E. Wimmer, ed.) Cold Spring Harbor Laboratory, Cold Spring Harbor, NY.

15. Young, J.A.T. (1994) The replication cycle of HIV-1. In: *The AIDS Knowledge Base.* (Cohen, P., Sande, M., Volberding, P., et al., eds.) Little Brown, New York, NY.

16. Federspiel, M.J., Bates, P., Young, J.A.T., Varmus, H.E., and Hughes, S.H. (1994) A system for tissue-specific gene targeting: Transgenic mice susceptible to subgroup A avian leukosis virus-based retroviral vectors. *Proc. Natl. Acad. Sci. USA.* 91: 11241-11245

17. Bélanger, C., Zingler, K., and Young, J.A.T. (1995) Importance of cysteines in the LDLR-related domain of the ALSV-A receptor for viral entry. *J. Virol.* 69: 1019-1024.

18. Zingler, K., Bélanger, C., Peters, R., Agard, D. and Young, J.A.T. (1995) Identification and characterization of the viral interaction determinant of the ALV-A receptor. *J. Virol.* , 69: 4261-4266

19. Zingler, K. and Young, J.A.T. (1996) Residue Trp-48 of Tva is critical for viral entry but not for high-affinity binding to the SU glycoprotein of Subgroup A avian leukosis and sarcoma viruses. *J. Virol.* 70: 7510-7516

20. Young, J.A.T. (1996) The replication cycle of HIV-1. In: *The AIDS Knowledge Base.* (Cohen, P., Sande, M., Volberding, P., et al., eds.) Little Brown, New York, NY in press.

21. Brojatsch, J., Naughton, J., Rolls, M.R., Zingler, K. and Young, J.A.T. (1996) CAR1, a TNFR-related protein is a cellular receptor for cytopathic avian leukosis and sarcoma viruses and mediates apoptosis. *Cell* 87: 845-855.

INVITED PRESENTATIONS (Meetings)

Invited Chair, Roundtable Discussion on Gene Therapies for AIDS, Second Annual NIH National AIDS Cooperative Drug Discovery and Development Meeting. California. 1988.

Invited Speaker, Banbury Conference on Receptor Mediated Virus Entry into Cells, Cold Spring Harbor Laboratory, 1991.

Invited Speaker, Keystone Symposium on Molecular Biology of Human Pathogenic Viruses. California, 1993.

Invited Speaker, Fifth Workshop on Pathogenesis by Non-acute Retroviruses. France, 1993.

Invited Speaker, Workshop on Immunology and Developmental Biology of the Chicken. Basel Institute of Immunology, Switzerland, 1994.

Invited Speaker, Sixth Workshop on Pathogenesis of Animal Retroviruses. Philadelphia 1994

Invited Speaker, Seventh Workshop on Pathogenesis of Animal Retroviruses. Seattle 1995.

Chair, Session on Receptors, Entry and Uncoating, Retroviruses Meeting at Cold Spring Harbor Laboratory, New York, 1996

Invited Speaker, FASEB Summer Conference on Principles in Viral, Bacterial, Fungal and Protozoan Pathogenesis. Colorado, 1996

Invited Speaker, FASEB Summer Conference on Virus Assembly, Vermont, 1996

Invited Symposium Speaker, American Society for Virology Symposium, Montana 1997

Invited Speaker, Cleveland Virology Symposium, 1997

Invited Speaker, Animal Cells and Viruses Gordon Conference, 1997

INVITED PRESENTATIONS (Institutions)

Department of Microbiology and Immunology, Penn State Medical Center, Hershey Pennsylvania, October 1996.

Department of Molecular Microbiology, Washington University at St. Louis School of Medicine, St. Louis, November 1996

Department of Microbiology, New York University Medical School, New York, January 1997

OTHER PRESENTATIONS

An attempt to specifically alter retroviral tropism using EGF-envelope chimeras. J.A.T. Young, P. Bates, H. Varmus. Poster presentation at Cold Spring Harbor RNA Tumor Viruses meeting. May 1988.

Transfer of susceptibility to ALSV infection into mammalian cells with chicken DNA. P. Bates, J.A.T. Young, and H.E. Varmus. Talk at Cold Spring Harbor RNA Tumor Viruses meeting. May 1989.

The human CD4 protein is efficiently incorporated into ALV particles. J.A.T. Young, P. Bates,

K. Willert, and H.E. Varmus. Talk at Cold Spring Harbor RNA Tumor Viruses meeting. May 1990.

An LDL receptor-related protein is the subgroup A ALV receptor. P. Bates, J.A.T. Young, H.E. Varmus. Talk at Cold Spring Harbor RNA Tumor Viruses meeting. May 1992.

Functional characterization of the subgroup A-Avian Leukosis Virus (ALV) receptor gene: Low levels of receptor expression are limiting for virus infection. J.A.T. Young, P. Bates, H.E. Varmus. Talk at Cold Spring Harbor RNA Tumor Viruses meeting. May 1992.

Mutational analysis of the cellular receptor for subgroup A-ALSV. K. Zingler, C. Bélanger, J.A.T. Young. Talk at Cold Spring Harbor Retroviruses meeting. May 1994.

A soluble version of the subgroup A-ALSV receptor blocks infection and binds directly to ALSV-A. L. Connolly, K. Zingler, J.A.T. Young. Talk at Cold Spring Harbor Retroviruses meeting. May 1994

An assay system to determine the relative levels of intermediate and complete DNA forms of HIV-1 DNA following infection. M. Jenkins, J. Naughton, J.A.T. Young. Poster presentation at Cold Spring Harbor Retroviruses meeting. May 1994

A putative receptor for cytopathic subgroups of ALSVs is a member of the Fas/TNFR protein superfamily. J. Brojatsch, J. Naughton, J.A.T. Young. Talk at Cold Spring Harbor Retroviruses meeting. May 1996.

Evidence that residue Trp-48 of TVA is involved at a step of viral entry other than binding the SU glycoprotein of subgroup A avian leukosis and sarcoma viruses. K. Zingler, J.A.T. Young. Talk at Cold Spring Harbor Retroviruses meeting. May 1996.

GRANTS

Characterization of ALSV-A Env/Receptor Interactions
NIH: 1R29CAAI62000-01A1
$615,301, July 1994 to June 1999

An Attempt to Target Retrovirus Vectors to Cells Expressing HIV-1 Envelope Proteins
AIDS Clinical Research Center, UCSF
One-year grant ($25,000). Funded January 26, 1994

Milton Fund ($12,000) Harvard Medical School, July 1995

Characterizing the Mechanisms of ALSV Entry into Cells
NIH: 1RO1CA70810-01
$ 985, 949 , July 1996 to June 2000.

OUTSIDE ACTIVITIES

1995 to present.	Consultant, Chiron Corporation, Emeryville, California
1995 to present.	Consultant, Vaccines and Related Biological Products Advisory Committee, Food and Drug Administration.